

REMARKS

Claims 1-9 and 11-16 are currently pending in the application. By this amendment, claims 1-9 are amended, claim 10 is cancelled, and new claims 11-16 are added for the Examiner's consideration. The foregoing separate sheets marked as "Listing of Claims" shows all the claims in the application, with an indication of the current status of each.

Applicant thanks Examiner for the indication that claims 5 and 6 would be allowable if rewritten to include all the limitations of base claim 1. New claims 15 and 16 reflect this indication, and are described fully in the section below entitled "Other Matters".

Objections: Specification

The Examiner has objected to the specification as lacking clear headings/divisions. Applicant has hereby amended the specification to include such headings, namely: Cross-Reference to Related Applications; Background of the Invention; Field of the Invention; Description of Related Art; Brief Summary of the Invention; Brief Description of the Drawings; and Detailed Description of the Invention.

The paragraphs that describe the drawings have been moved (by deleting those paragraphs from pages 8 and 9 and inserting those paragraphs, together with the heading "Brief Description of the Drawings" after the "Summary" section.

A new Abstract has been provided on a separate sheet. The abstract is substantially identical to that of International patent application PCT/EP2003/007892 (to which the present application claims priority) except that references to "novelty" have been removed, as is required for abstracts.

The paragraph located at lines 7-17 on page 1 has hereby been replaced with a replacement paragraph in which the word "lipopeptides" is correctly spelled, as required by Examiner.

Applicant submits that none of these amendments add new matter to the specification, being entirely formal in nature, and respectfully request reconsideration and withdrawal of all objections to the specification.

Objections: Claims

Examiner has objected to claim 1 as unclear due to the recitation describing R3. Claim 1 has hereby been amended to recite that R3 is a covalently bonded polyethylene glycol (polyoxyethylene) $-(CH_2-CH_2-O)_m-CH_2-CH_2-X$, and the possible equivalents of X are clearly recited, thereby rendering clear the subject matter of this claim.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of this objection.

Claim Rejections: 35 USC § 112, 2nd

Claim 1 stand rejected under 35 USC § 112, second paragraph, as indefinite. In particular, the Examiner states that the recitation that “several radicals” may be “different” is unclear.

Claim 1 has hereby been amended to clearly recite that $R = H$, benzyl-, or C_{1-6} alkyl, where, when $X = NR_2$, the R groups can be identical or different. Applicant submits that this amendment renders the meaning of this portion of claim 1 definite, and respectfully requests reconsideration and withdrawal of this rejection.

Claim Rejections: 35 USC § 112, 2nd and 101

Claim 10 has hereby been rejected under 35 USC § 112, second paragraph, as indefinite, and under 35 USC 101 as drawn to nonpatentable subject matter. Claim 10 has hereby been cancelled, thereby making moot this rejection.

In view of the foregoing, Applicant requests reconsideration and withdrawal of this rejection.

Claim Rejections: 35 USC § 112, first paragraph

Claims 1-4 and 7-10 stand rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. This rejection is traversed.

Claim 10 has hereby been cancelled, thereby making moot this portion of the rejection.

Regarding claim 1, the Examiner states that the generic phrase “bisacryloxypolyglycine conjugate” is not sufficiently described, and the specification does not clearly define or provide examples of what qualify as compounds of the invention.

Claim 1 has hereby been amended to precisely recite the subject matter that is being claimed. The claim now recites that R_1 and R_2 can be identical or different and are C_8-C_{22} alkyl,

alkenyl or alkynyl fatty acid radicals which are bonded by way of the carboxyl group; Y = -NH-, -O-, -S-, or -OCO-; and R₃ is a covalently bonded polyethylene glycol (polyoxyethylene) -(CH₂-CH₂-O)_m-CH₂-CH₂-X, where X = OR, NR₂, SR or COOR, and R = H, benzyl-, or C₁₋₆ alkyl, where multiple R groups can be identical or different. No functional characteristics are now recited in the claims, and the feature of R₃ being substituted once, twice or several times has been eliminated. Further, the positions of the variable groups are definite in this description.

R1 and R2 are identical or different and are C₈-C₂₂ alkyl, alkenyl or alkynyl fatty acid radicals which are bonded by way of the carboxyl group. As pointed out by the Examiner, two exemplary compounds with attached fatty acids (both palmitoyl) are described in the Examples. However, Applicant submits that the chemical structure of fatty acids in general and the chemical reactions of fatty acids were well-known in the art at the time the application was filed. In fact, the literature is replete with references that were available to those skilled in the art at the time the present application was filed. For example, *Fatty Acid and Lipid Chemistry* by F.D. Gunstone (Chapman and Hall) was published in 1996. One of skill in the art would be well acquainted with protocols for the attachment of fatty acids in positions R1 and R2, as depicted in Formula 1 of the application. Further, a description of an exemplary synthesis is provided on page 9 at lines 1-11 of the application. In addition, a description of another known fatty acid compound is provided on page 2 at lines 1-15. Applicant submits that given the plethora of information available at the time of filing of the application coupled with the teaching of the application, the claims are fully enabled for all fatty acid radicals.

In addition, Applicant notes that claims 5 and 6, which Examiner has indicated contain patentable subject matter, recite that the bisacyloxypropylcysteine conjugate of the invention is a S-[2,3-bis(acyloxy)-(2S)-propyl]-L-cysteinyldicarboxypolyethylene glycol. "Acyloxy" is not restricted to a particular fatty acid radical.

With regard to the water-soluble polymer radical, the radical is precisely defined as covalently bonded polyethylene glycol (polyoxyethylene) -(CH₂-CH₂-O)_m-CH₂-CH₂-X. Various embodiments of the invention include: where the molecular weight of the polyethylene glycol moiety is from 100 to 30000 daltons (claim 3), preferably from 100 to 500 (new claim 11) and m is preferably from 5 to 700 (claim 4). Applicant notes that each of these claims has hereby been

amended to eliminate confusing language and to provide direct reference to the polyethylene glycol moiety. Applicant therefore submits that the subject matter of claims 1-4 and 7-9 has, by such amendments, been rendered clear and enabled for the scope of the invention as presently claimed.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of this rejection.

Other matters

New claim 11 recites that, in the bisacyloxypropylcysteine conjugate of claim 4, m is from 100 to 500. Applicant submits that no new matter is added in this claim since the subject matter of claim 11 is taken directly from original claim 4. Claim 4 has hereby been amended to eliminate the “preferably” clause, and the embodiment of m = 100 to 500 is now properly separated from claim 4 as dependent claim 11.

New claims 12 and 13 recite that the bisacyloxypropylcysteine conjugate of claims 5 and 6, respectively, is S-[2,3-bis(palmitoyloxy)-(2S)-propyl]-L-cysteinylcarboxypolyethylene glycol. Applicant submits that new claims 12 and 13 do not add any new matter, since the subject matter of each claim is taken directly from original claims 5 and 6. Accordingly, the language of claims 5 and 6 has been amended to eliminate the “preferably” clause, and the material from the clause is now properly presented in dependent claims 12 and 13.

New claim 14 has been added to the application to capture the subject matter of cancelled claim 10. New claim 14 recites, in accord with US patent practice, a method of stimulating an immune response to an antigen in an animal or human. The method comprises the step of simultaneously administering to the animal or human the antigen and a bisacyloxypropylcysteine conjugate according to formula 1. Applicant submits that this new claim does not add any new matter, its subject matter being an adaptation of the subject matter of claim 10 to a form that is accepted in US patent practice. Further, the subject matter of new claim 14 is fully enabled. Amendments have hereby been made to the description of formula 1 which render definite the identity of the compounds which are encompassed by the formula. Claim 14 recites a method a method of stimulating an immune response to an antigen in an animal or human. Examples 3 and 4 of the application describe experiments in which demonstrate the stimulation of an immune

response upon simultaneous administration of an antigen and a compound of formula 1 of the invention. In Example 3, a robust humoral IgA immune response was elicited at both systemic and mucosal levels. In Example 4, an effective T cell mediated proliferation response was elicited when a compound of the invention was utilized as a mucosal adjuvant. Therefore, Applicant submits that successful use of the method recited in claim 14 (stimulation of an immune response to an antigen by simultaneously administering the antigen and a bisacyloxypylcysteine conjugate according to formula 1) is amply demonstrated in these Examples.

Examiner has indicated that the subject matter of claim 5 and 6 is allowable, if rewritten to include all the features of base claim 1. New claims 15 and 16 are hereby added to the application. New claims 15 and 16 include the subject matter of claim 1 and that of claims 5 and 6, respectively. Applicant submits that new claims 15 and 16 should thus be allowable.

Applicant respectfully requests consideration and allowance of new claims 11-14.

Finally, claims 1 and 7 have been amended to distinguish the " R_2 " moiety of Formula 1 from the " R_2 " moiety of " NR_2 ", which is a possible equivalent of X, by placing brackets around R in NR_2 , yielding $N[R]_2$. This convention has also been adopted in new claims 14-16 and adds no new matter, being entirely formal in nature.

Concluding Remarks

In view of the foregoing, it is requested that the application be reconsidered, that claims 1-9 and 11-14 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400 (fax: 703-787-7557; email: ruth@wcc-ip.com) to discuss any other changes deemed necessary in a telephonic or personal interview.

If an extension of time is required for this response to be considered as being timely filed, a conditional petition is hereby made for such extension of time. Please charge any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Ruth E. Tyler-Cross', with a stylized flourish at the end.

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